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Veas, Cecilia, Crispi, Francisca and Cuadrado, Cristóbal orcid.org/0000-0002-0174-5958 (2021) Association between gender inequality and population-level health outcomes:Panel data analysis of organization for Economic Co-operation and Development (OECD) countries. *EClinicalMedicine*. 101051. ISSN: 2589-5370

<https://doi.org/10.1016/j.eclinm.2021.101051>

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Research Paper

Association between gender inequality and population-level health outcomes: Panel data analysis of organization for Economic Co-operation and Development (OECD) countries

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ARTICLE INFO

Article History:

Received 3 May 2021

Revised 7 July 2021

Accepted 14 July 2021

Available online xxx

Keywords:

Gender inequality

Gender inequality index

Health inequality

ABSTRACT

Background: Gender plays a well-recognized role in shaping health inequities. However, the population-level health consequences of gender inequalities have not been measured comprehensively. The goal of this study was to evaluate the association between gender inequality and health indicators in organization for Economic Co-operation and Development (OECD) countries.

Methods: Ecological study based on 1990–2017 panel data for OECD member countries. Gender inequality was measured using the Gender Inequality Index (GII). The population health parameters evaluated were life expectancy (LE), healthy life expectancy (HALE), years of life lost (YLL), years lived with disability (YLD), disability-adjusted life years (DALYs), and specific-cause mortality. Two-way fixed-effects linear models were used to assess the relationship between gender inequality and health outcomes. Models included potential mediating and confounding factors such as health spending, political model, and income inequalities.

Findings: Greater gender inequality was associated with lower LE (-0.49% ; $CI_{95} -0.63\% - -0.31\%$; p -value < 0.0001), HALE (-0.47% ; $CI_{95} -0.63\% - -0.31\%$; p -value < 0.0001) and with increased premature mortality YLL (6.82% ; $CI_{95} 3.63\% - 10.75\%$; p -value < 0.0001) and morbidity measured in DALYs (1.50% ; $CI_{95} 0.48\% - 2.46\%$; p -value $= 0.0028$) and YLD (2.59% ; $CI_{95} 0.67\% - 4.77\%$; p -value $= 0.0063$) for each 0.1 increments on the GII. The sensitivity analysis indicated that the results were robust to the various specifications of the causal models.

Interpretation: Our results suggest that gender inequality pose a sizable impact on population health outcomes. Promoting gender equality as part of public policies is vital for optimizing health on a population scale.

Funding: Agencia Nacional de Investigación y Desarrollo (ANID)/Programa Becas/Magister Becas Chile/2017–22,170,332

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1. Introduction

Sex is understood as the biological characteristics that differentiate males from females [1,2], while gender is a social construct that defines roles, behaviors, activities, cultural conventions, and attributes assigned to men and women by society [1,2]. These constructs influence power structures and norms. The masculine gender is typically favored [1,2], giving rise to gender inequities.

Such inequalities have been present in different societies, as evidenced by gaps in power, resources, and rights, with diverse and cross-sectional implications [1,2]. Many international organizations have endeavored to balance the scales: the United Nations

Development Programme (UNDP), for instance, has adopted to “Gender Equality” as its 5th Goal in the Sustainable Development Goals (SDGs) 2015–2030 [3,4].

Gender has been recognized as a social determinant of health (SDH) [1], and as such, socioeconomic and political contexts exert a powerful influence on gender constructs [1,2]. Several gender theories have been used in public health research [5]. In this study, we applied gender relations, life circumstances and gender roles as main approaches. When an infant born, is immediately immersed into a gender system, where all the determinants and structures interacts with “axes of power and privilege to shape an individual’s overall social position in relation to others” [2]. The relation between gender and the other SDH its closely related with the concept of *intersectionality*, introduced by Crenshaw in 1989 [6], which explain that given the intersections of the different modalities of domination, it is not

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Research in context

Evidence before this study

We searched PubMed to identify studies using the search terms (gender OR sex) AND (inequality OR equality OR inequity OR equity OR disparity) AND health. A recently published systematic review of the effect of gender inequality on health (King, 2020), the most compressive to date, suggest that study findings varied significantly among different health indicators and conditions, with some reporting negative effects on mortality and morbidity patterns. Few studies were available analyzing potential impacts on life expectancy or years of healthy life lost. Furthermore, to our knowledge, no prior studies analyzed consistently the effect of gender inequality on other relevant population-level health indicators such as years of life lost, years lived with disability, or disease burden in the general population.

Added value of this study

This panel data analysis demonstrates a relationship between gender inequality and a wide-range of population-level health indicators in OECD nations between 1990 and 2017. Health outcomes assessed included life expectancy, years of healthy life, years of life lost, years lived with disability, and disease burden, allowing for first time a global yet detailed perspective on the impact of gender inequality on population health. It should be noted that the majority of these variables had not been analyzed previously. This study also provides analytical models that demonstrate the effects of governance, income inequalities, and health spending on population-level health outcomes, as well as the inter-relation between these variables and gender inequality.

Implications of all the available evidence

These results suggest that reducing gender inequality could improve health outcomes at a population scale, resulting in increased overall and healthy life expectancy and decreasing years of life lost, years lived with disability, and disease burden, in the general population, and in men as well as women. This supports the need to develop gender-sensitive public policies, for the benefit of the whole society. Finally, these findings suggest new lines of research to explore other elements that may affect health at a population scale, including morbidity patterns and behavioral risk factors.

health research, and clinical data collection [1,2,13,15,16]. Gender-linked differences in health outcomes are apparent across the life-span, contributing to disparities in rates of avoidable mortality and morbidity [1,13–15,17]. Women face a greater risk of depression and anxiety-related disorders [13,18,19]. Women also tend to be diagnosed later and treated less aggressively for cardiovascular diseases [15,19]. Breast, cervical, and uterine carcinomas are the most prevalent cancers in women despite being highly preventable, reflecting gaps in healthcare access [13,19]. Men, in turn, are more vulnerable to violence-related mortality (accidents, homicides, drug abuse), [16,17] suicide (with a three to four times higher risk), and health risk behavior-related diseases (lung cancer, cirrhosis) [8,13,16,17,19]. Research suggests that these disparities may be linked to gender stereotypes [8,16].

Social, behavioral, and biological factors also seem to affect the gap in life expectancy between men and women (with women living longer than men) [13–15,17,20,21]. While an estimated two years of this difference is attributable to biological factors [21], the difference is closer to five years in most organization for Economic Co-operation and Development (OECD) member countries [17]. However, it would be limiting to reduce the analysis to the single parameter of survival, as health encompasses many factors, such as specific-cause mortality, morbidities, risk factors, and disabilities [13–15,17,19,21].

Given the above findings, can we quantify the effect of gender inequality on population-level health parameters? We certainly have resounding evidence of the link between gender inequalities and health outcomes [1,8,22–29,13,14,16–21], and several studies have measured the effect of these inequalities on parameters such as life expectancy (LE), obesity, cancer, and risk behaviors [26–29]. However, to our knowledge, no study has provided a comprehensive quantitative analysis of the association between gender inequality and other parameters such as healthy life expectancy (HALE), years of life lost (YLL), years lived with disability (YLD), disability-adjusted life years (DALYs), or mortality for specific causes such as suicide, lung cancer, or cervical cancer.

The objective of this study is to analyze the association between gender inequality and health parameters in OECD nations. We hope that our findings will improve our understanding of the impact of gender inequalities and allow us to estimate the magnitude of this effect on population-level health outcomes.

2. Methods

2.1. Study design

This study analyzed the relationship between gender inequality and population-level health in OECD countries, using the Gender Inequality Index (GII) developed by the United Nations Development Programme (PNUD) [30]. A longitudinal analysis based on 1990–2017 panel data for OECD nations was performed. These countries were selected due to their comparability and availability of data for the years to be analyzed [31]. The study uses population-level, publicly available data and therefore ethical approval was not required.

2.2. Variables and data sources

2.2.1. Exposure

There are many indicators that reflect population-level gender inequities, and many composite indices have been developed to address the multidimensionality of the phenomenon [26,32,33]. The GII is the most widely-used such measure in the literature [26–29,34]. This index evaluates gender inequality along three dimensions: reproductive health (maternal mortality, adolescent birth rate), empowerment (proportion of men and women with at least some secondary education, proportion of men and women

possible analyze one kind of inequality without looking the other, because none by itself is capable of generating a complete understanding of the situation [6,7].

Researchers have explored gender as a determinant of social structures and behavior patterns that affect well-being on a population scale [1,2]. Such studies have identified numerous ways in which these patterns provoke gender inequalities in health [1,2,8]. Some emphasize that there are direct pathways in the generation of health inequities, which are acquired in a cumulative burden over the course of life, as well as with the direct influence of other social and structural determinants [2]. In this way, gender inequalities can impact health outcomes through different mechanisms influencing mortality and morbidity patterns across populations and, therefore, it is a relevant object of study for public health [1,2,9–14].

Gender inequalities are associated with differential health-risk behavior patterns and lifestyle choices, healthcare access, gender biases in health systems, and inequities in resource distribution,

occupying parliamentary seats), and economic status (labor market participation among men and women) [30] (see Supplementary Material 1 for further details). This index has a range that goes from 0 to 1, where 0 means gender equality, and 1 represents total inequality in all the dimensions measured for one gender. The index is designed to penalize more those countries that are worse off in all dimensions [30]. In addition to its wide adoption in the literature, the index was selected due to data availability, considering that it cover all OECD countries in all the years it was measured (1995, 2000, 2005 y 2010–2017), and comprehensiveness, its cover 80% of the dimensions that United Nations suggests for Gender Statistics (see Table S1 for further details on index selection) [30,35].

2.2.2. Outcomes

The health indicators evaluated were Life Expectancy (LE), Health Adjusted Life Expectancy (HALE), disability-adjusted life years (DALY), years lived with disability (YLD), and years of life lost (YLL). We also examined specific-cause mortality for suicide, lung cancer, and cervical cancer. The first two causes of death are theoretically associated with gender-linked health-risk behaviors, and mortality due to cervical cancer serves as an specific indicator of healthcare access for women [8,13,16,17,19]. Data for the general population and disaggregated by sex were extracted from OECD [25] and Global Burden of Disease Study (GBD) [36].

2.2.3. Other variables of interest

As differences in health outcomes are attributable to many factors beyond gender inequality, we also characterized each country according to political, economic, and sociocultural variables with a potential impact on the health of the population. Gini index was used to measure income inequality [37]. The Polity IV Project (p_polity2) Quality of Government index (QoG) [38] was used to measure political structure. QoG scores range from 0 to 10, where 0 is least and 10 most democratic (see Supplementary Materials 2). Public spending on health was measured in international dollars adjusted for purchasing power parity (ppp_gsalud) [37]. Data for study variables was extracted for the period analyzed. As information for some of the years in the series was not available, multiple imputation was used for data missing at random, obtaining a balanced panel for analysis. More information regarding the missing data analysis and imputation process is available in Supplementary Materials 3.

2.2.4. Statistical analysis

Two way-fixed effect linear regression models were used, with fixed effects for country (k) and time in years (t) to adjust for unobserved characteristics of each unit of analysis (country) and time-period. We performed Hausman test to inform model selection between fixed- and random-effects model specifications (see Supplementary Materials 4 for details).

Three models were proposed, based on known associations among the selected variables, using causal directed acyclic graphs (DAG) to identify minimal sufficient adjustment sets [39]. Model 1 included Gini as a confounding variable for the effect of gender inequality on health outcomes, with a minimally-sufficient adjustment set that included health spending ($\text{Log}(y_{jkt}) = \beta_1 G_{kt} + \text{GINI}_{kt} + \text{ppp_gsalud}_{kt} + X + T + e_{kt}$) (see Supplementary Materials 5). This model was used to analyze each outcome variable (y_{jkt}), with separate adjusted models for the general population, men, and women.

The outcome variables were log-transformed to improve the goodness-of-fit of the models and to allow for estimation of percent change by each unit of GII. We calculated the proportional effect of each 0.1-point change in gender inequality (GII) on each outcome variable ($\text{proportional effect} = (e^{\beta_1} - 1) * 100 / 10$), using 95% confidence intervals based on robust standard errors. R software v3.6.0 was used to perform the data analysis and design the graphs.

2.3. Sensitivity analysis

Models 2 and 3 were used to analyze the sensitivity of our results to various assumptions. Model 2 included Gini as a confounding variable for the effect of gender inequality on health outcome, with a minimally-sufficient adjustment set that included type of government (gov, measure with The Polity IV Project (p_polity2)) ($\text{Log}(y_{jkt}) = \beta_1 G_{kt} + \text{gov}_{kt} + X + T + e_{kt}$). Model 3 included Gini as a mediating variable for the effect of gender inequality on health outcome, with a minimally-sufficient adjustment set that included type of government ($\text{Log}(y_{jkt}) = \beta_1 G_{kt} + \text{GINI}_{kt} + \text{gov}_{kt} + X + T + e_{kt}$). The DAGs for these models are available in Supplementary Materials 5. Both models were used to analyze each outcome variables (y_{jkt}), with separate adjusted models for the general population, men, and women.

2.4. Role of the funding source

This study was funded by the former National Commission for Scientific and Technological Research (CONICYT) and current National Research and Development Agency of Chile (ANID)/Scholarship Program/Magister Becas Chile grant 2017–22,170,332. The funding source had no role in study design, data collection, analysis, or interpretation of results. All the authors had access to the full dataset and were responsible for the final decision to submit the manuscript for publication.

3. Results

The analysis of the 36 OECD countries (1990–2017) included 1008 country-year observations Table 1, provides an overview of the results for individual variables. The average GII score was 0.18

Table 1
Results by study variable.

Variable	Mean	SD	p-value
<i>Exposure variables</i>			
Gender inequality index	0.18	0.12	..
GINI	33.12	5.92	..
Health spending*	2419.4	1583.79	..
<i>Outcome variables</i>			
Life expectancy: Population	77.68	3.52	..
Life expectancy: Men	74.51	4.25	< 0.0001
Life expectancy: Women	80.79	2.96	..
Healthy life expectancy: Population	67.12	2.88	..
Healthy life expectancy: Men	65.13	3.62	< 0.0001
Healthy life expectancy: Women	69.06	2.25	..
Years of life lost: Population	5045,636	8306,098.27	..
Years of life lost: Men	2961,826	4812,288.01	< 0.0001
Years of life lost: Women	2075,033	3471,645.83	..
Disability-adjusted life years: Population	28,411	5308.07	..
Disability-adjusted life years: Men	30,916	7226.13	< 0.0001
Disability-adjusted life years: Women	26,073	3834.70	..
Years lived with disability: Population	3952,452	6650,187.72	..
Years lived with disability: Men	1777,367	2998,223.78	0.0072
Years lived with disability: Women	2177,215	3645,598.70	..
Suicide mortality: Population	14.68	8.37	..
Suicide mortality: Men	24.18	14.83	< 0.0001
Suicide mortality: Women	6.57	3.78	..
Lung cancer mortality: Population	45.09	12.19	..
Lung cancer mortality: Men	76.25	24.91	< 0.0001
Lung cancer mortality: Women	23.1	11.61	..
Cervical cancer mortality	6.71	2.96	..

This table shows the descriptive statistics (mean and standard deviation) for the variables used for the analysis. $n = 1008$ for each exposure variable and the outcomes variables. A t -test was performed to compare outcomes variables between men and women. *Median in international dollars adjusted for purchasing power parity.

Table 2

Associations between gender inequality and population-level health outcomes.

Outcome	GII: general population	p-value	Adjusted R ²	GII: men	p-value	Adjusted R ²	GII: women	p-value	Adjusted R ²
LE	−0.49% *** (−0.63%–−0.31%)	<0.0001	0.97	−0.55% *** (−0.73%–−0.37%)	<0.0001	0.97	−0.48% *** (−0.62%–−0.033%)	<0.0001	0.96
HALE	−0.47% *** (−0.63%–−0.31%)	<0.0001	0.96	−0.52% *** (−0.70%–−0.31%)	<0.0001	0.97	−0.40% *** (−0.54%–−0.28%)	<0.0001	0.95
YLL	6.82% *** (3.63%–10.75%)	<0.0001	0.98	6.82% *** (3.63%–10.75%)	<0.0001	0.98	6.65% *** (3.50%–10.54%)	<0.0001	0.99
DALYs	1.50% ** (0.48%–2.46%)	0.0028	0.90	1.85% *** (0.73%–3.10%)	0.00081	0.92	0.96% * (0.14%–1.85%)	0.021	0.88
YLD	2.59% ** (0.67%–4.77%)	0.0063	0.99	2.46% ** (0.78%–4.48%)	0.0032	0.99	2.59% ** (0.93%–4.48%)	0.0015	0.99
Suicide mortality	2.21% (−1.56%–7.86%)	0.29	0.80	3.50% (−0.54%–9.16%)	0.099	0.81	3.50% (−0.84%–10.14%)	0.13	0.79
Lung cancer mortality	−1.22% (−2.52%–3.91%)	0.12	0.86	−1.04% (−2.88%–1.27%)	0.34	0.86	−0.14% (−2.05%–2.21%)	0.9	0.88
Cervical cancer mortality	—	—	—	—	—	—	0.62% (−1.13%–2.71%)	0.51	0.93

This table shows the effect of GII on the different health parameters on general population, men and women analyzed for the model 1, which used GINI as a confounding variable for the effect of gender inequality on health outcome, with a minimally-sufficient adjustment set that included type of government. Estimators represents percentage change (%) for each outcome per 0.1-point change in GII on the outcome variable: $(\exp(\text{coef})-1)*100/10$. *** $p < 0.011$; ** $p < 0.01$; * $p < 0.5$. $n = 1008$ observations for each variable. LE: Life Expectancy; HALE: Health Adjusted Life Expectancy; YLL: years of life lost; YLD: years lived with disability; DALYs: disability-adjusted life years.

(SD = 0.12). Women had greater average LE, HALE, and YLD than men, as well as more favorable DALYs and YLL scores. Mortality rates for suicide and lung cancer were higher among men. The average mortality rate for cervical cancer was 6.71 (SD = 2.96) (Table 1).

In Model 1, gender inequality was negatively associated with LE and HALE (Table 2). For each 0.1-point increase in GII, LE decreased by 0.49% in the general population (CI₉₅ 0.63–0.31%; p -value < 0.0001). This is equivalent to a 0.38-year reduction of the life-expectancy for an average country within our sample. In the case of

men and women, for each 0.1-point increase in GII, LE decreased by 0.49% (CI₉₅ 0.73–0.37%; p -value = 0.00039), and 0.48% (CI₉₅ 0.62–0.033%; p -value < 0.0001), respectively (Fig. 1).

For each 0.1-point increase in GII, HALE decreased by 0.47% in the general population (CI₉₅ 0.63–0.31%; p -value < 0.0001), 0.52% in men (CI₉₅ 0.70–0.31%; p -value < 0.0001), and 0.40% in women (CI₉₅ 0.54–0.28%; p -value < 0.0001) (Fig. 1). While the estimated magnitude of the effect was greater in men than women, we could not reject the null hypothesis that the effects were equal.

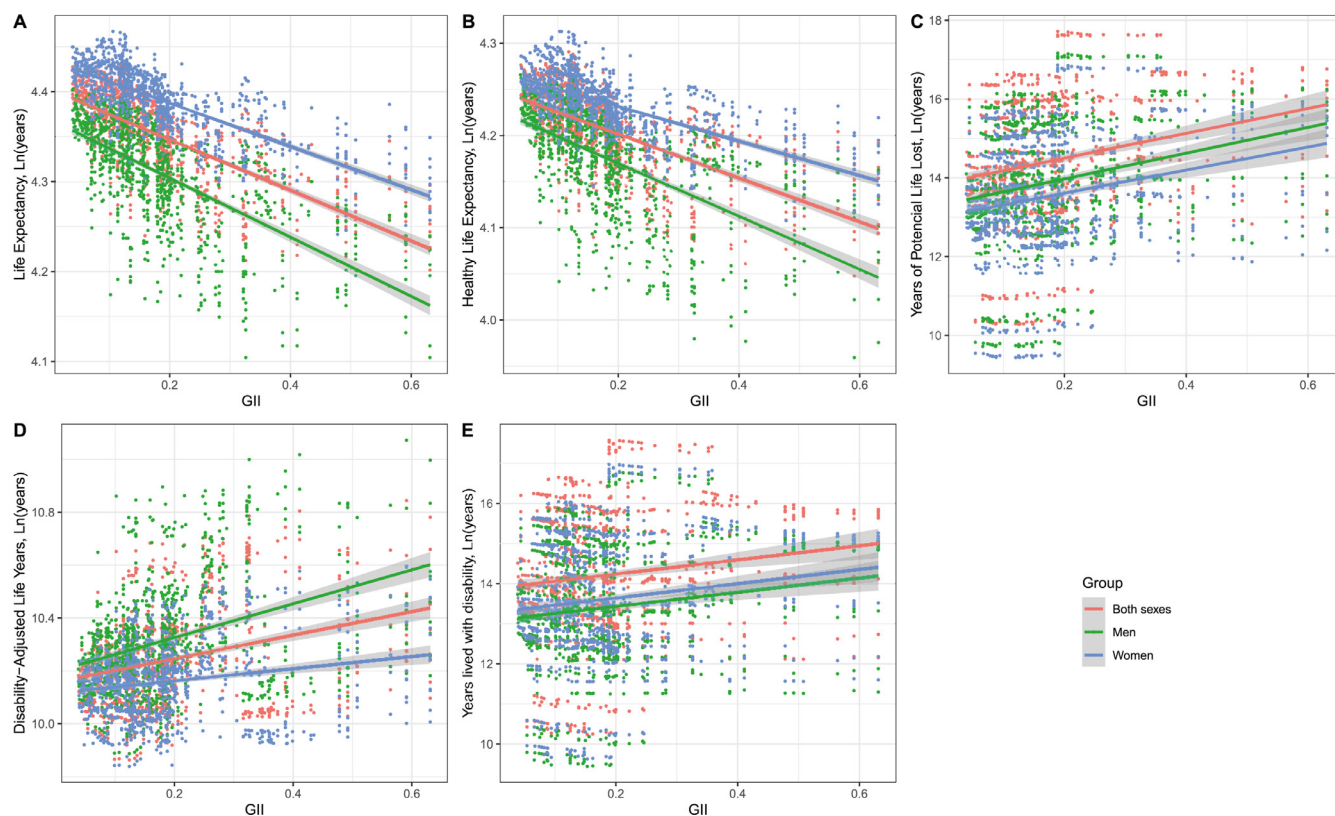


Fig. 1. Associations between GII and health outcomes. This figure shows the effect of GII on the different health parameters analyzed for the model 1, which used GINI as a confounding variable for the effect of gender inequality on health outcome, with a minimally-sufficient adjustment set that included type of government. GII: Gender Inequality Index. Figures show linear regression of associations between GII and health outcomes. (a): Life Expectancy; (b): Healthy Adjusted Life Expectancy; (c): Years of Life Lost; (d): Disability-Adjusted Life Years; (e): Years Lived with Disability. Green line: men; blue line: women; red line: both sexes (general population).

Greater gender inequality was positively associated with the health parameters YLL, DALYs, and YLD (Table 2). Increases in GII were reflected in increased premature mortality (YLL) in the general population (6.82%; CI₉₅ 3.63–10.75%; *p*-value < 0.0001), men (6.82%; CI₉₅ 3.63–10.75%; *p*-value < 0.0001), and women (6.65%; CI₉₅ 3.50–10.54%, *p*-value < 0.0001) (Fig. 1). Higher GII scores were also associated with greater disease burden (DALYs) in the general population (1.50% CI₉₅ 0.48–2.46%; *p*-value = 0.0028), men (1.85%; CI₉₅ 0.73–3.10%; *p*-value = 0.00081), and women (0.96%; CI₉₅ 0.14–1.85%; *p*-value = 0.021) as well as with and disability (YLD) in the general population (2.59%; CI₉₅ 0.67–4.77%; *p*-value = 0.0063), men (2.46%; CI₉₅ 0.78–4.48%, *p*-value = 0.0032), and women (2.59%; CI₉₅ 0.93–4.48%; *p*-value = 0.0015).

There was no significant association between gender inequality and suicide, lung cancer, or cervical cancer mortality (see Supplementary Materials 6).

The sensitivity analysis (Models 2 and 3) indicated that the results were robust to the various specifications of the causal models (see Supplementary Materials 6) and a complete case analysis (see Supplementary Materials 7).

4. Discussion

This study shows for first time the effects of gender inequality across a wide range of population health indicators. Our results suggest that gender inequality has a negative impact on the population health. Greater gender equity is robustly associated with more favorable outcomes for YLL, DALYs, and YLD in all of the models tested, both for the general population and for men and women separately. Similarly, greater gender equity was also associated with more favorable figures for HALE and LE, suggesting that gender equity decreases premature mortality, disease burden, and years lived with disability. Furthermore, overall and healthy life expectancy were longer in nations with greater gender equity.

One hypothesis to explain these results is that gender inequality, in terms of parity of education, representation, and healthcare access, may be associated with the differences in how gender norms, stereotypes and inequalities have affected men and women historically [2]. While reduction of gender inequalities improves living conditions and health status among women, these gendered stereotypes and inequalities across life are thought to exacerbate premature mortality, disease burden, and years lived with disability among men [1,8,19,20,26]. Gender stereotypes of masculinity linked with risky behaviors, violence and help-seeking conducts are expectedly challenged in more gender-equal societies. Therefore, reducing gender inequality could benefit both men and women. Moreover, these results are consistent with research that has proposed a convergence of health outcomes for men and women in contexts of greater gender equity [26]. Interestingly, our analysis suggests that improving equity may have a greater impact on the health of men than women, and that the gap between sexes decreases under the assumption of gender equity (Fig. 1A,B–D). This finding supports the concept that social constructs may play a greater role than biological factors in the gaps between men and women that are observed in most countries for parameters such as life expectancy [17,20,21,28,29].

A major strength of this study is the robustness of the results. The analysis included a large number of countries and a long span of time, and therefore the results reflect diverse social and temporal contexts [31–33]. Furthermore, gender inequality was measured with an index used widely in the literature [26–29,34]. Finally, applying three models allowed us to observe the behavior of gender inequality in various scenarios. This study analyzed the data for a wide range of health outcomes, and the results were robust to the various specifications of the causal models.

These advantages help to ameliorate the potential limitations of this work. First, it should be noted that this study had a gender binary

approach for reasons of feasibility. The analysis was limited to gender gaps between men and women, omitting other identities. Addressing non-binary identities remains challenging as the validated indices available to measure gender inequality do not include multiple gender identities or orientations. This shortcoming represents a major pending task in the study of the field of gender inequality. Also, GII does not measure intersectionality of gender in its methodology and does not cover the influence of social gender norms in this area. New gender indexes has been proposed more recently, offering a more comprehensive inclusion of this aspects (such SIGI and GSNI) [40,41]. Since these indexes are relatively new, covering a shorter period of time, its analytical value is still limited. Nevertheless, it will be interesting to study the effects of gender inequality measured by indexes on health in future research. Second, as the study is observational, the results cannot be used to draw causal conclusions regarding the associations identified. While we adopted a rigorous approach in designing the study models, adjusting for observable and non-observable variables, it is not possible to rule out the possibility that other confounding factors not included in the analysis may at least partly underlie the findings. Third, given that this was an ecological study, caution should be used in extrapolating the results to the individual level; phenomenon observed on the collective scale are not necessarily transferrable to individuals.

Future research should explore the effect of gender inequality on other health outcomes, as well as its role in behavioral or risk factors related to various morbidities. In addition, it would be helpful to identify causal links between gender inequality and health inequalities. Finally, testing these findings in other countries would be informative.

These results provide a broad perspective on gender in the context of public health policy. Our findings underscore the need to target the indicators included in the GII index as these areas are critical for addressing gender inequalities in the population [30]. This study demonstrates a significant association between gender inequality and population health parameters, with effects that impact men at least as much as women. Greater gender equity is associated with more favorable YLL, DALYs, and YLD values as well as greater LE and HALE. Promoting gender equality in public policies and decision-making, therefore, is vital for optimizing health on a population scale.

Contributors

All authors contributed with the conceptualization, investigation, methodology and formal analysis. CV wrote the original manuscript and CC and FC contributed with the writing – review & editing. CV, FC and CC verified the underlying data.

Declaration of Competing Interest

CVP reports a scholarship from the Agencia Nacional de Investigación y Desarrollo (ANID)/Programa Becas/Magister Becas Chile/2017- 22,170,332, during the study; CC reports fundings for the Project Redressing Gendered Health Inequalities of Displaced Women and Girls in contexts of Protracted Crisis in Central and South America (ReGHID) from ESRC-UKRI (ES/T00441X/1), during the study; FC has no competing interest to declare.

Funding

CVP was funded by the former National Commission for Scientific and Technological Research (CONICYT) and current National Research and Development Agency of Chile (ANID)/Scholarship Program/Magister Becas Chile gran 2017-22179332. CC was funded by the project Redressing Gendered Health Inequalities of Displaced Women and Girls in contexts of Protracted Crisis in Central and South America (ReGHID), funded by ESRC-UKRI (ES/T00441X/1). The funding source

had no role in the study design, data collection, analysis, or interpretation of results. Only the authors have access to the full dataset, and the authors are responsible for the final decision to publish.

Data sharing statement

The dataset used for this article is freely available within the supplementary material. Any queried can be directed to the corresponding author.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.eclinm.2021.101051.

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